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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,103	11/05/2001	A. James Mixson	5627*5	7244

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EXAMINER	
NGUYEN, DAVE TRONG	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,103	MIXSON, A. JAMES	
	Examiner	Art Unit	
	Dave T Nguyen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,2,4-14 and 16-44* is/are rejected.

7)☒ Claim(s) *3 and 15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11/5/01* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 27-44 have been added by the preliminary amendment dated November 5, 2001.

In view of Applicant's response, dated October 30, 2003, the group restriction requirement has been withdrawn by the examiner. While the species restriction is maintained for the reasons of record, the prior art of record does not teach or suggest SEQ ID NO: 5 or any other specific sequences as recited in the claims, the species restriction has also been withdrawn by the examiner.

Claims 1-44 are pending.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-13, 15-44, are readable on a generic transport polymer are recited in the base claims, wherein at least 10% of the amino acid residues are histidine, at least 10% of the amino acid resides are non-histidine, and wherein the generic claim has a markush group of negative limitations, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification and the state of the prior art of record provide sufficient description of a delivery composition comprising a pharmaceutical agent and a transport

cationic polymer comprising at least 10% of the amino acid residues being histidine, and at least 10% of residues being lysine and glycine residues, and wherein the polymer enhances the transport of a pharmaceutical agent to the interior of a cell. However, it is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or assays for making the polymer genus as claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of polymeric conjugates and/or functional groups thereof that must exhibit the disclosed biological functions as contemplated by the as-filed specification.

It is not sufficient to support the present claimed invention by disclosing only a co-polymer comprising histidine residues and lysine residues because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any and/or all other polymeric conjugates having other unspecified residues in addition with the at least 10% of histidine residues positioned at a particular primary seqeunce with the biological functions as contemplated by the specification and the claims. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which is not conventional in the art as of applicants effective filing date. Claiming a genus of an enormous number of transport polymers, with a mere description of the presence of at least 10% histidine residues being present, without a description of a common structure of the essential domain of the transport polymer in order to carryout the transporting

property as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of the claimed polymeric complexes that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, In view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 1-2, 5-13, 15-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to:

a delivery composition comprising a pharmaceutical agent and a transport polymer comprising at least 10% of the amino acid residues being histidine, and at least 10% of residues being lysine residues, and wherein the polymer enhances the transport of a pharmaceutical agent to the interior of a cell.

The specification does not reasonably provide enablement for the presently pending claims encompassing any and/or all other polymeric delivery vectors including those that embrace therapeutic applications as recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Specifically, since the claimed invention is not supported by a sufficient written description (for possessing of the genus of polymeric transporting complexes as recited in the claims, particularly in view of the reasons set forth above, one skilled in the art would not known how to use and make the claimed invention so that it would operate as intended, *e.g.* functions as a nucleic acid delivery vector that exhibits all of the biological functions as recited in the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-2, 4, 7-13, 15, 18-25, 27-31, 34-43 are rejected under 35 U.S.C. 102(e) as being anticipated by PACK et al (US 2001/0006817 A1).

With respect to claims readable on a delivery composition comprising a pharmaceutical agent and a transport linear or branced copolymer comprising at least 10% of the amino acid residues being histidine, and at least 10% of residues being lysine residues, and wherein the polymer enhances the transport of a pharmaceutical agent to the interior of a cell, PACK teaches the same or mainly a single linear or branched copolymer composed mainly of polysine and polyhistidine throughout the reference, *e.g.,* see par. 0011 on page 2, par. 0036, par. 0038-0044, and figures 5A and 5B. Nucleic acids are disclosed on par. 0044. Method of delivery and making of the polymer complex or conjugate together with a pharmaceutical agent is also disclosed throughout the working examples.

Thus, PACK anticipates the claims.

Claims 1, 2, 4-13, 15-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over PACK et al (US 2001/0006817 A1) taken with either Hawley-Nelson, US pat No. 6,051,429 or Tomalia (US 6,475,994).

With respect to claims readable on a delivery composition comprising a cationic lipid or a transitional metal, a pharmaceutical agent and a transport linear or branced copolymer comprising at least 10% of the amino acid residues being histidine, and at least 10% of residues being lysine residues, and wherein the polymer enhances the transport of a pharmaceutical agent to the interior of a cell, PACK teaches the same throughout the reference, *e.g.,* see par. 0011 on page 2, par. 0036, par. 0038-0044, and par. 0100. Nucleic acids are disclosed on par. 0044.

PACK does not teach that the delivery composition could further comprising a nucleic acid intraceullarly delivery enhancer such as a cationic lipid or a transitional metal, however, the concept of utilizing a cationic lipid or a transitional metal enhancer/polymer complex to enhance the intracellular delivery of a nucleic acid is well recognized in the art, as evidenced by applicant's background information as disclosed on page 15 of the specification, columns 14-15 of Hawley-Nelson, or Tomalia on column 9, respectively.

As such, it would have been obvious for one of ordinary skill in the art to have further employed any intracellular delivery enhancer such as a transitional metal/polymer conjugate or a cationic lipid in the delivery composition of PACK. One of ordinary skill in the art would have been motivated to do so because the concept of utilizing a cationic lipid or a transitional metal enhance/polymer conjugate to enhance

the intracellular delivery of a nucleic acid is well recognized in the art, as evidenced by applicant's background information as disclosed on page 15 of the specification, columns 14 and 15 of Hawley-Nelson, or Tomalia on column 9, respectively.

Thus, the claimed invention as a whole was *prima facie* obvious.

Claims 1, 2, 4-13, 15-44 are rejected under 35 USC 103(a) as being unpatentable over PACK taken with either Hawley-Nelson, US pat No. 6,051,429 or Tomalia (US 6,475,994), and further in view Gopal.

To the extent that the claims are readable on a polyhistidine/polysine copolymer which further comprises a spacer composed of glycine residues so as to interconnect the copolymer to other components in the composition without causing stearic interference among the delivery components such as nucleic acid, cationic lipids and/or polymeric delivery components, PACK taken with either Hawley-Nelson, US pat No. 6,051,429 or Tomalia (US 6,475,994) are applied here as indicated above. PACK taken with either Hawley-Nelson, US pat No. 6,051,429 or Tomalia (US 6,475,994) silent as to the use of glycine residues in the copolymer, however, Gopal teaches that spacer composed of neutral amino acid residues such as glycine residues can be used to interconnect peptide domains and nucleic acid domains so as to enhance a peptide-mediated gene transfer into a target cell.

Thus, it would have been obvious for one of ordinary skill in the art to employ glycine residues in the copolymer of PAC taken with Hawley-Nelson or Tomalia. One would have been motivated to do so as to interconnect peptide domains and nucleic

acid domains, thereby enhancing a peptide-mediated gene transfer into a target cell without causing a stearic interference among the delivery components in the delivery composition.

Thus, the claimed invention as a whole was *prima facie* obvious.

Claims 3 and 15 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **571-272-0731**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Amy Nelson*, may be reached at **571-272-0804**

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Trong Nguyen
Primary Examiner
Art Unit: 1632

DAVE T. NGUYEN
PRIMARY EXAMINER